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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
FRONDA, CHRISTIAN L

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 08/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/975,813	MILLER ET AL.	
	Examiner	Art Unit	
	Christian L. Fronda	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-54* is/are pending in the application.

4a) Of the above claim(s) *26-30 and 33-52* is/are withdrawn from consideration.

5)☒ Claim(s) *3,5,6,24 and 25* is/are allowed.

6)☒ Claim(s) *4,7-23,31,32,53 and 54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 3-54 are pending in the application. Claims 26-30 and 33-52 have been withdrawn from consideration.

2. Claims 3-25, 31, 32, 53, and 54 are under consideration in this Office Action.

3. The rejection of claims 15 and 16 under 35 U.S.C. 102(b) as being anticipated by Fosang et al. (FEBS Lett. 1996 Feb 12;380(1-2):17-20); and GenBank Accession NP_037359 and NP_001126) as evidenced by Fosang et al. (Biochem. J. (1989) 261, 801-809) has been withdrawn in view of applicants' amendment to the claims filed on 05/11/2006.

4. The rejection of claim 4 under 35 U.S.C. 102(b) as being anticipated by Doege et al. (J Biol Chem. 1991 Jan 15;266(2):894-902; and Accession A39086. 10-Sep-1999) has been withdrawn in view of applicants' amendment to the claims filed on 05/11/2006.

5. The rejection of claim 7 under 35 U.S.C. 102(b) as being anticipated by Antonsson et al. (Accession A34234 20-March-1992) has been withdrawn in view of applicants' amendment to the claims filed on 05/11/2006.

6. The rejection of claims 8, 9, 11-14, 17-21, 31, and 32 under 35 U.S.C. 103(a) as being unpatentable over Fosang et al. (FEBS Lett. 1996 Feb 12;380(1-2):17-20) in view of Koritsas et al. (Anal Biochem. 1995; 227: 22-26) has been withdrawn in view of applicants' amendment to the claims filed on 05/11/2006.

7. The rejection of claims 10, 22, and 23 under 35 U.S.C. 103(a) as being unpatentable over Fosang et al. in view of Koritsas et al. as applied to claims 8, 9, 11-14, 17-21, 31, and 32, and further in view of Duan et al. (Anal Biochem. 1994 Feb 1;216(2):431-8) has been withdrawn in view of applicants' amendment to the claims filed on 05/11/2006.

Claim Rejections - 35 U.S.C. § 112, 2nd Paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 8-14, 31, 32, 53 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants' arguments filed 05/11/2006 have been fully considered but are not persuasive. The examiner agrees with applicants' argument that the phrase "wherein the P1 amino acid residue" has adequate antecedent basis, but respectfully disagrees with applicants' position that the phrase "ADMP-sensitive Glu^{373}-Ala^{374} bond" is definite (claims 31 and 32) and a sequence identifier is not necessary since that the plain language of claim 53 and the specific recitation of the ADMP cleavage sites in an isolated aggrecan peptide fragment identifies the metes and bounds of the claimed invention.

By recitation of the phrase "Glu^{373}-Ala^{374} bond" in claims 31 and 32, it is not clear if applicants are actually referring to SEQ ID NO: 1. The Sequence Listing discloses that SEQ ID NO: 1 consists of only 40 amino acids. It appears that this bond is actually at positions 20 and 21 of SEQ ID NO: 1 and SEQ ID NO: 2. If applicants are referring to this specific bond, then appropriate correction is requested which states positions 20 and 21 of SEQ ID NO: 1 and SEQ ID NO: 2.

Because the claim recites "wherein said numbering corresponds to the numbering of human aggrecan protein", it is not clear if applicants are referring to SEQ ID NO: 1, SEQ ID NO: 3, or any other amino acid sequence of a wild-type, mutant, or variant of the human aggrecan protein. No specific SEQ ID NO of the amino acid sequence having the ADMP-susceptible cleavage site between the amino acid pairs selected from the group consisting of "Glu^{373}-Ala^{374} , E^{1545}-G^{1546}, E^{1714}-G^{1715}, E^{1819}-A^{1820}, and E^{1919}-L^{1920} "is recited. If applicants are referring to the wild-type human aggrecan protein, then recitation of its amino acid sequence by SEQ ID NO may overcome the rejection.

In regard to dependent claims 8-14, the phrase "wherein the peptide has a linking moiety" renders the claim vague and indefinite. Independent claims 3-7 recite "fragment **consisting** of" (emphasis added). However, dependent claims 8-14 broaden the scope of the independent claims 3-7. Amending the dependent claims to recite the phrase "further comprising a linking moiety" may overcome the

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out

his invention.

11. Claims 8-23, 31, 32, 53, 54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants' arguments filed 05/11/2006 have been fully considered but are not persuasive. Applicants' position is that the claims recite the common structural feature of an ADMP specific susceptible cleavage site and that recitation of the term "aggrecan" conveys distinguishing information to those skilled in the art at the time of filing. The examiner respectfully disagrees for reasons of record as supplemented below.

The claims are genus claims encompassing many aggrecan peptide fragments of any function, amino acid sequence, and structure having any aggrecan degrading metallo protease (ADMP)-susceptible cleavage site of any amino acid sequence and structure. While the specification discloses SEQ ID NOs: 1-6, there is no recitation in the claims of any function that is common to the claimed genus. For example, the claims do not recite that the peptide fragments inhibit the enzymatic activity of an ADMP as disclosed in the specification. Thus, one skilled in the art cannot visualize or recognize the identity of the members of the claimed genus.

In view of the above considerations, one of skill in the art would not recognize that applicants were in possession of a genus of aggrecan peptide fragments of any function, amino acid sequence, and structure having any ADMP-susceptible cleavage site of any amino acid sequence and structure.

12. Claims 4, 7-23, 31, 32, and 53 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated human aggrecan peptide consisting of the amino acid sequence of SEQ ID NO:1 or SEQ ID NO: 3, does not reasonably provide enablement for any aggrecan peptide from any source or peptide fragment having any function, amino acid sequence, and structure comprising or an amino acid sequence that is 80% identical to amino acids 1-40 of SEQ ID NO: 1 or SEQ ID NO: 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants' arguments filed 05/11/2006 have been fully considered but are not persuasive. Applicants' position is that one of ordinary skill in the art at the time the application was filed would have readily designed and synthesized sequences having the claimed percentage identity and used the disclosure to evaluate the activity of the claimed peptides. The examiner respectfully disagrees for reasons of record as supplemented below.

As stated in the previous Office Action and further explained here, general teaching

regarding screening and searching for the claimed invention is not guidance for making the claimed invention. While the specification provides guidance and examples for making a peptide consisting of the amino acid sequence of SEQ ID NO: 1 or SEQ ID NO: 3, knowledge regarding the biological utility of the claimed peptides and the specific amino acid residues to change without affecting biological activity of the claimed peptides or peptide fragment is lacking. The claims do not recite that the peptide fragments have a specific biological activity, such as inhibiting the enzymatic activity of an ADMP as disclosed in the specification.

Thus, trial and error experimentation must be performed either by searching a vast number of biological sources from which to isolate the peptide or peptide fragment, searching and screening for a biological activity of the peptide, such as inhibiting the enzymatic activity of an ADMP as disclosed in the specification; or screening and searching for any amino acid in SEQ ID NO: 1 or 3 to change (amino acid insertion, deletion, addition, substitution, or combinations thereof) that does not affect biological activity in order to make an amino acid sequence that is 80% identical to SEQ ID NO: 1 or 3. Without specific guidance for the specific amino acid residues to change in SEQ ID NO: 1 and the biological activity of the claimed peptides, the amount of experimentation to make and/or use the invention is undue.

Conclusion

13. Claims 3, 5, 6, 24, 25 are allowed.

14. Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N

Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

16. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free): If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CLF

TEKCHAND SAIDHA
PRIMARY EXAMINER